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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,802	12/26/2001	Marc Zabeau	29314/34158A	2002

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,802	ZABEAU ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. This action is in response to Applicants' response, filed on April 29, 2004. Currently, claims 1-23 are pending and remain rejected. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn. Specifically, the objections to Claims 2, 7 and 15 have been overcome by Applicants' amendments.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-10 and 12-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Zabeau et al. (EP 534858 A1, cited in the IDS).

With respect to Claims 1 and 12, Zabeau teaches a method for detecting an endonuclease site polymorphism in DNA comprising:

a) isolating sample DNA;

b) deriving a set of concomitantly amplifiable target DNA fragments from the sample DNA;

c) treating the target DNA fragments obtained in step (b) with a probe restriction endonuclease reagent;

d) amplifying the probe restriction endonuclease reagent treated target DNA fragments of step c);

e) analyzing the DNA of step d) to determine which target fragments are amplified and/or which target fragments are not amplified; and wherein target DNA fragments which are amplified lack a recognition sire for the probe restriction endonuclease reagent and target fragments having a recognition site for the probe restriction endonuclease reagent are not amplified.

(see abstract, pg. 3, lines 20-46 and pgs. 6-11, for example)

With respect to Claims 2-5, Zabeau teaches the concomitantly amplifiable target DNA fragments of step b) are "derived" by treatment of four and six base cutting endonucleases (see Examples 2-6, for example).

With respect to Claims 2-5, it is noted that step c)'s "treating" step can be interpreted as either adding an additional endonuclease or the treatment of the target DNA fragments with endonucleases already present in the assay. For example, Zabeau teaches that following the derivation of the concomitantly amplifiable target DNAs using a first and a second restriction endonuclease and the ligation of adaptors, the restriction endonucleases are still active and thus the target DNAs are still being "treated" with the endonucleases (see pg. 14, ln. 35-37) (see also pg. 18, lines 1-3 and pg. 21, lines 53 to pg. 22, teaching two distinct treatment steps).

With respect to Claim 6, Zabeau teaches preparing primers, which flank the endonuclease site polymorphism (ESP) for use in amplifying, said concomitantly amplifiable target DNA fragments (pgs. 6-9, for example).

With respect to Claims 7 and 15-16, Zabeau teaches the concomitantly amplifiable DNA fragments are modified by the ligation of adapters to both termini of said fragments and then amplified by PCR (see pg.6 and Examples 2-6, for example).

With respect to Claim 8, Zabeau teaches the ligation of adaptors (pg. 6, for example).

With respect to Claims 9-10, Zabeau teaches the probe restriction endonuclease has a recognition sequence of four or six nucleotides (see Examples 2-6).

With respect to Claims 13-14, it is an inherent property that that the site polymorphism will is an alteration which is either recognized and cut by the probe restriction endonuclease reagent or eliminates a recognition sequence for said probe restriction endonuclease reagent.

With respect to Claim 17, Zabeau teaches that the amplified products are hybridized to probes (pg. 11, for example).

With respect to Claims 18-23, the broadest reasonable interpretation is that the claims are drawn to any probe DNA fragment having an ESP, which comprises any fragment susceptible to endonuclease digestion.

Specifically, with respect to Claims 18-19, Zabeau teaches the probe DNA fragments are derived by digestion of sample DNA with one or more sampling restriction endonuclease reagents (see Examples 2-6).

With respect to Claims 20-23, the DNA fragments are derived by digestion of a pool of sample DNAs obtained from a plurality of individuals (see abstract, Examples 5-6 and pg. 8, for example).

Applicants Arguments

Applicants argue Claims 1 and 18 require a first fragmentation step (using a restriction endonuclease), and a second endonuclease-based fragmentation step, steps b and c, respectively. See page 13 of Applicants response. Furthermore, Applicants argue that Zabeau et al. "neither explicitly or inherently contemplates a method that uses at least two separate endonuclease-based steps as required in the format of the present claims." See page 13 of Applicants response.

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive for several reasons. First, Applicants are arguing limitations not required by the claims. Neither Claim 1, nor Claim 18 specifically requires two separate endonuclease-based steps. In Claim 1, step c is the only step in Claim 1 that requires treatment with a restriction endonuclease. Furthermore, Claim 18 does not specifically require any treatment steps with a restriction endonuclease. Claim 18 recites, "[a] method for obtaining probe DNA fragments for use in detecting endonuclease site polymorphisms, the method comprising: (a) isolating sample DNA; (b) deriving a set of concomitantly amplifiable target DNA fragments from the sample DNA; (c) selecting from the target DNA fragments, probe DNA fragments having an endonuclease site polymorphism (ESPS) for the probe restriction endonuclease." This claim does not require any active endonuclease-based treatment steps, let alone two separate endonuclease-based steps.

Even assuming the claims did require two endonuclease-based steps, which they do not, Zabeau teaches the use of two endonuclease-based treatments. See Examples 2-6 and rejection above. Accordingly, the rejection is maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zabeau et al. (EP 534858 A1, cited in the IDS), as applied to claims 1-10 and 12-23 above, and further in view of Wang et al. (Science (1998) 280: 1077-1081, cited in the IDS), and further in view of Mead et al. (WO 94/21663, cited in the IDS).

The teachings of Zabeau are presented above. Specifically, Zabeau teaches a method for detecting an endonuclease site polymorphism in DNA comprising using probe restriction endonucleases having recognition sequences of short nucleotide sequences, but Zabeau does not teach restriction endonucleases having recognition sequences of 2 nucleotides.

Wang teaches a high percentage of single nucleotide polymorphisms occur within CpG dinucleotides, and thus the analysis of CpG dinucleotides are advantageous in detecting polymorphisms (see pg. 1078).

Mead teaches digesting DNA with a probe restriction endonuclease reagent, CGase I, which cleaves DNA at the dinucleotide CpG (see pgs. 1 and 77, for example).

Accordingly, in view of the teachings of Wang and Mead, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Zabeau so as to have treated a target DNA fragment with a probe restriction endonuclease reagent having a recognition sequence of two nucleotides, such as CGase I, in order to have achieved the benefit of providing a more effective means of detecting single nucleotide polymorphisms due to the high level of polymorphisms located within CpG dinucleotides.

Applicants Arguments

Applicants argue that because Zabeau alone or in combination with Wang or Mead do not teach two separate endonuclease-based fragmentation steps, Claim 11 (sic) is unobvious over the cited art. See Applicants response on pages 14-15.

Response to Applicants Arguments

Applicants' arguments have been considered, but are not persuasive because the claims do not require two separate endonuclease-based fragmentation steps, and even assuming the claims did, Zabeau teaches two separate endonuclease-based fragmentation steps. See above.

Conclusion

8. No claims are allowable.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Alexander H. Spiegler
August 12, 2004

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